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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/784,645	Applicant(s) EMPEDOCLES ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13,16-24 and 27-43* is/are pending in the application.

4a) Of the above claim(s) *27-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,16-24 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 9 September 2002 in Paper No. 14 in which claims 1, 3, 8, 9, 19, 21 and 40-42 were amended and claims 11, 12, 14, 15, 25 and 26 were canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 12 dated 9 May 2002 under 35 U.S.C. 112, second paragraph and under 35 U.S.C. 103(a) are withdrawn in view of the amendments. The previous objections to Claims 25, 40 and 42 are withdrawn in view of the amendments. The previous rejections in Paper No. 12 under 35 U.S.C. 102(e) and Double Patenting are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

Claims 1-10, 13, 16-24 and 40-43 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 1-10, 13, 16-24 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Bawendi et al (U.S. Patent No. 6,306,610 B1, filed 17 September 1999).

Regarding Claim 1, Bawendi et al disclose a method of detecting a ligand comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distance locations to provide an array wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspecting of containing the first ligand wherein the first ligand is linked through a linker to a first semiconductor nanocrystal after the contacting under conditions in which the first ligand binds specifically to the first anti-ligand to form a first complex; removing unbound ligand from the array; and identifying the location of the first complex by detecting the presence of the first complex of the first semiconductor nanocrystal thereby indicating the presence of the first ligand of interest (Column 22, lines 48-65 and Fig. 2).

Regarding Claim 2, Bawendi et al disclose the method wherein the linker comprises two members of a binding pair a first member attached to the first ligand and a second member attached to the first semiconductor (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 3, Bawendi et al disclose the method wherein the sample contains a second ligand linked to a second semiconductor nanocrystal which is detectably distinct from the first semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to forma second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Regarding Claim 4, Bawendi et al disclose the method of Claim 1 wherein the anti-ligands are nucleic acid probes and the first ligand is a target nucleic acid (Column 5, line 18-26).

Regarding Claim 5, Bawendi et al disclose the method of Claim 3 wherein the anti-ligands are nucleic acid probes and the first ligand is a target nucleic acid (Column 5, line 18-26 and Column 26, lines 15-46).

Regarding Claim 6, Bawendi et al disclose the method comprising oligonucleotides (i.e. antiligands) immobilized onto an array and contacting the array with probes (i.e. ligands) wherein the probes are linked to the semiconductor nanocrystal prior to the contacting step (Column 26, lines 15-46, especially, lines 17-22 and 36-40).

Regarding Claim 7, Bawendi et al disclose the method comprising first and second oligonucleotides (i.e. antiligands) immobilized onto an array and contacting the array with probes (i.e. ligands) wherein the probes are linked to the semiconductor nanocrystal prior to the contacting step (Column 26, lines 15-46, especially, lines 41-46 and multiplex assay).

Regarding Claim 8, Bawendi et al disclose the method wherein the first ligand bears a single first semiconductor nanocrystal (Column 26, lines 41-46).

Regarding Claim 9, Bawendi et al disclose the method wherein the first ligand and the second ligand bear a single first and second semiconductor nanocrystal (Column 26, lines 41-46).

Regarding Claim 10, Bawendi et al disclose the method wherein the linker comprises two members of a binding pair a first member attached to the first ligand and a second member attached to the first semiconductor (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 13, Bawendi et al disclose the method wherein the nucleic acid probes are allele-specific i.e. single nucleotide polymorphism (Column 20, lines 23-27)

Regarding Claim 16, Bawendi et al disclose the method wherein the plurality of anti-ligands are proteins (Column 5, lines 9-17).

Regarding Claim 17, Bawendi et al disclose the method wherein the ligand is a proteins (Column 5, lines 9-17).

Regarding Claim 18, Bawendi et al disclose the method wherein the anti-ligands are antibodies (Column 5, lines 9-17).

Regarding Claim 19, Bawendi et al disclose the method of Claim 16 wherein the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to form a second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Regarding Claim 20, Bawendi et al disclose the method wherein the anti-ligand is a component of a tissue specimen e.g. antibodies, proteins and nucleic acids (Column 5, lines 9-26).

Regarding Claim 21, Bawendi et al disclose the method of Claim 16 wherein the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to forma second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Regarding Claim 22, Bawendi et al disclose the method wherein the anti-ligand is selected from the group consisting of proteins and nucleic acid targets and the ligands are selected from the group consisting of antibodies and nucleic acid probes (Column 5, lines 9-26).

Regarding Claim 23, Bawendi et al disclose the method wherein the anti-ligands are distinct target nucleic acids and the ligands are nucleic acid probes (Column 8, lines 22-28).

Regarding Claim 24, Bawendi et al disclose the method wherein the anti-ligands are proteins and the ligands are proteins (Column 5, lines 9-17).

Regarding Claim 40, Bawendi et al disclose a method comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distinct locations thereon to provide a first array, wherein the plurality comprises a first anti-ligand that is a binding partner of a first ligand; contacting the first array with a sample containing or suspected of containing the first ligand whereby the first ligand and the first anti-ligand interact to form a first complex; labeling the first ligand in the first complex with a first semiconductor nanocrystal; and identifying with location of the array includes the first complex by detecting the presence of therein of the first semiconductor nanocrystal (Column 22, lines 48-67).

Regarding Claim 41, Bawendi et al disclose the method wherein the first plurality of anti-ligands comprises a second anti-ligand that is a binding partner of a second ligand; the sample contains or is suspected of containing the second ligand such that the second ligand and the second anti-ligand form a second complex; labeling the second ligand in the second complex with a second semiconductor nanocrystal that is detectably distinct form the first semiconductor nanocrystal; and determining which location on the array include the first complex, the second complex or both by detecting the presence of the nanocrystals (Column 22, line 59-Column 23, line 7).

Regarding Claim 42, Bawendi et al disclose the method wherein the first ligand comprises a first member of a first binding pair and the semiconductor nanocrystal is linked to a second member of the first binding pair through a linker (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 43, Bawendi et al disclose the method wherein the second ligand comprises a first member of a second binding pair and the second semiconductor nanocrystal

is linked to a second member of the second binding pair (Column 7, lines 8-18 and Claims 3-4).

Response to Arguments

4. Applicant argues that Bawendi et al do not teach or suggest an array in which a ligand is immobilized at positionally distinct locations on a solid support are claimed in both independent Claims 1 and 40. Applicant further argues that Bawendi et al do not teach or suggest identifying the locations on the array of a complex by detecting the presence in the complex of a semiconductor nanocrystal. The arguments have been considered but are not found persuasive because the claims are drawn to a plurality of antiligands immobilized on a solid support at positionally distinct locations and because Bawendi et al teach, describe and illustrate the claimed plurality of antiligands immobilized at positionally distinct locations as claimed. First, Bawendi et al teach "a series of different antibodies is covalently linked to a substrate." (Column 22, lines 60-61). Covalent linkage of antibodies to a substrate immobilizes antibodies at positionally distinct locations because each antibody is immobilized and positioned at the location of its covalent linkage. More than one antibody cannot be covalently linked at the exact same location. Therefore, Bawendi et al's covalently linked "series of different antibodies" are immobilized on a solid support at positionally distinct locations as claimed. Second, Bawendi et al illustrate antiligands immobilized at positionally distinct locations (see Fig. 1 and 2). Finally, Bawendi et al discuss immobilization of antiligands wherein they teach a preferred method of immobilization consists of a solid support wherein antiligands are immobilized to allow separation of the antiligands (Column 26, lines 15-35). For the reasons given above, Bawendi et al clearly disclose the invention as claimed.

Regarding Claim 40, Applicant argues that the instant claims require labeling of the ligand after the ligand has interacted with the antiligand on the array to form a complex and as such the differ from Bawendi et al wherein the ligands are labeled before contacting the antiligand. The argument has been considered but is not found persuasive because in contrast to Applicant's assertion, Bawendi et al specifically teach labeling of the ligand after binding the antiligand. As cited above, Bawendi et al covalently link antibodies (antiligands) to the substrate; antibody-specific antigens (ligands) are added to the immobilized antibodies; and finally, antibodies labeled with nanocrystals are bound to the antibody-antigen(ligand) thereby labeling the antigen (ligand) after the antigen (ligand) has interacted with the antibody (antiligand) on the array (Column 22, lines 59-65 and Fig. 2). Therefore, Bawendi et al clearly disclose the invention as claimed.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-10, 16-26 and 40-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,274,323 B1 in view of Koster (U.S. Patent No. 5,606,789, issued 25 February 1997). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods for detecting a target molecule by detecting fluorescence emitted by a semiconductor nanocrystal and differ only in the patent claims being drawn to the a single species of target molecule (i.e. polynucleotide) a single species of affinity moiety (i.e. PCR product) various species of first and second binding members (e.g. avidin and streptavidin, digoxygenin and anti-dioxygenin) while the instant claims are drawn to the genus ligand, anti-ligand and first and second binding pairs. The courts have stated that a genus is obvious in view of the teaching of a species (see; In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) and MPEP 2131.02). Therefore, the instantly claimed methods drawn to the genus target molecule and affinity moiety are obvious in view of the patent methods drawn to the species. The sets of claims differ also in the that instant claims are

drawn to immobilized anti-ligand. However, immobilized anti-ligands were well known in the art at the time the claimed invention was made as taught by Koster who teach a similar method of detecting a target molecules wherein the anti-ligand is immobilized whereby detection of the anti-ligand is facilitated (Column 7, lines 19-29 and 54-56). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the patent detection by immobilizing the anti-ligand as instantly claimed because one of skill in the art would have been motivated to immobilized the anti-ligand to thereby facilitate target detection as taught by Koster (Column 7, lines 54-56).

Response to Arguments

7. Applicant states that a terminal disclaimer to overcome the above obviousness-type double patenting rejection will be filed upon notification of allowable subject matter. Applicant's intent to file a terminal disclaimer is acknowledged. The rejection is maintained.

8. Claims 1-10, 16-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 12-15 of copending Application No. 09/784,866. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods for detecting targets immobilized on a substrate using the same method steps i.e. by detecting a semiconductor nanocrystal (quantum dot) and differ only in the instant claims being drawn to the drawn to the detecting a "ligand" while the '866 application is drawn to detecting a "target species". However, the instantly claimed "ligand" (Claims 4, 16-19 and 21) and the '866 "target species" (Claim 10) are both selected from the group consisting of nucleic acids, proteins, antibodies and aptamers. Therefore the sets of claims are essentially the same

and differ only in the arrangement and grouping of the claim limitations. Hence, the instant claims are obvious in view of the '866 claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 1-10, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 17-22, 28-39 of copending Application No. 09/766,273. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations i.e. immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the'273 claims are drawn to a species of ligand and anti-ligand (i.e. polynucleotide) while the instant independent claims are broadly drawn to the genus ligand and anti-ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand and anti-ligand (i.e. genus) is obvious in view of the '273, polynucleotide (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-10, 13-15, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 09/882,193. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations. Both sets of claims are drawn to method comprising the steps of immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the'193 claims are drawn to a species of ligand and anti-ligand (i.e. target nucleic acid and complementary primer) while the instant independent claims are broadly drawn to the genus ligand and anti-ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand and anti-ligand (i.e. genus) is obvious in view of the '193, target nucleic acid and complementary primer (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1-10, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25, 27-29, 32, 35-39 and 53 of copending Application No. 09/887,914. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations i.e. immobilizing an anti-ligand, contacting the immobilized

anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the'914 claims are drawn to a species of ligand (i.e. polymerase chain reaction product) while the instant independent claims are broadly drawn to the genus ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand (i.e. genus) is obvious in view of the '914, polymerase chain reaction product (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Applicant's comments

12. Regarding the above provisional obviousness-type double patenting rejections over copending Applications 09/784,866; 09/766,273; and 09/882,193, Applicant requests that the rejections be held in abeyance pending notification of allowable subject matter. Applicant's request is acknowledged. The rejections are maintained.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
November 7, 2002